ISSN: 2320-2882

IJCRT.ORG



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Review On Pharmaceutical Benefits Of *Trigonella Foenum-Graecum*

¹M. L. MAdhuri, ²N.V.L. Suvarchala V, ³M. Mamatha, ⁴K. Ramu, ⁵T. Sampath Reddy, ⁶Md Sayyaf, ⁷G. Madhu

^{1,3}Assistant professor, ²Professor, ^{4,5,6,7}Scholar
¹Department of pharmaceutical chemistry,
¹Gokaraju Rangarju College of Pharmacy, Hyderabad, India

Abstract: Herbs have high medicinal value in Indian homes and proved to arrest, reduce and terminate most of the disease by the use of active constituents prepared out of them. Among these, fenugreek (*Trigonella foenum-graecum* L.) is an important herb which has been recognized as an imperative medicinal plant by various scientists around the world. According to the literature analysis, the presence of various bioactive compounds such as alkaloids, flavonoids, saponins, fibers, fatty acids, etc. contributes to the therapeutic potential of the herb. In this study after a general discussion of chemical constituents, the biological and pharmacological actions of fenugreek such as Anti-diabetic activity, Antilipedimic activity, Anti-oxidant activity, Anticancer activity, Immunomodulatory activity and other pharmaceutical uses were briefly reviewed. Due to its medicinal value, the extracts/powders from different parts of fenugreek have been effectively utilized in food and pharmaceutical industries. Accordingly, the present review is an attempt to highlight the important pharmaceutical benefits and curative applications of fenugreek as an effectual therapeutic agent against different diseases.

Index Terms - Trigonella foenum-graecum, phytochemistry, pharmaceutical benefits

Introduction

Fenugreek, Trigonella Foenum-groecum Linne, is an annual herb indigenous to the countries bordering on the eastern shores of the Mediterranean and largely cultivated in India, Egypt, and Morocco [1]. The name fenugreek comes from foenum-graecum, meaning Greek hay, asthe plant was traditionally used to scent inferior hay [2]. The name of the genus, Trigonella, is derived from the old Greek name, denoting 'three-angled', [3, 4] probably refering to the triangular shape of the flowers. The first recorded use of fenugreek is described on an ancient Egyptian papyrus dated to 1500 B.C. Fenugreek seed is commonly used in cooking [5]. Fenugreek has strong flavor and aroma. The plants leaves and seeds are widely consumed in Indo-Pak subcontinent as well as in other oriental countries as a spice in food preparations, and as an ingredient in traditional medicine [6]. A wide range of uses were found for fenugreek in ancient times. Medicinally it was used for the treatment of wounds, abscesses, arthritis, bronchitis, ulcer and digestive problems. Traditional Chinese herbalists used it for kidney problems and conditions affecting the male reproductive tract. Fenugreek was, and remains, a food and a spice commonly eaten in many parts of the world [3].

Fenugreek is also considered as a rich source of dietary fibre and other important nutrients needed for proper growth and development. Studies have also affirmed the nutraceutical and physiological properties of fenugreek which support the potential applications of fenugreek in developing numerous functional food products and pharmaceutical products.[7] As fenugreek is rich in several phytochemicals, alkaloids, carbohydrates, steroidal saponins, amino acids and minerals are present in fenugreek, it can be used for nutritional, nutraceutical, medicinal and therapeutic purposes.[8] Fenugreek has been extensively used as a flavour enhancer in several traditional cuisines. Additionally, the medicinal properties of fenugreek such as anticarcinogenic, antidiabetic, antioxidant, hypocholesterolemic, anti-lithogenic antimicrobial and immunological properties, make it an important compound to be used in food and pharmaceutical industries.[9] In addition to the medicinal properties of fenugreek, it has also been used as an emulsifier and stabilizer in different types of food products. Moreover, use of fenugreek extracts or powders has also been reported for developing bakery and extruded products.[10]

I. PHYTOCHEMISTRY

Fenugreek contains a number of chemical constituents including steroidal sapogenins. Diosgenin component has been found in the oily embryo of fenugreek. There are two furastanol glycosides, F-ring opened precursors of diosgenin that have been reported in fenugreek also as hederagin glycosides. Alkaloids such as trigocoumarin, nicotinic acid, trimethyl coumarin and trigonelline are present in stem. The mucilage is a standing out constituent of the seeds.[11] There is about 28% mucilage; a volatile oil; 2 alkaloids such as trigonelline and Choline, 5% of a stronger-smelling, bitter fixed oil, 22% proteins and a yellow coloring substance are present in stem (Grieve, 1984). Fenugreek contains 23-26% protein, 6-7% fat and 58% carbohydrates of which about 25% is dietary fiber (US Department of Agriculture, 2012). Fenugreek is also a rich source of iron, containing 33 mg/100 g dry weight (US Department of Agriculture, 2001). 1.1% fiber, and 6% carbohydrates. The mineral and vitamins present in leaves include calcium, zinc iron, phosphorous, riboflavin, carotene, thiamine, niacin and vitamin C. [12][13] found that fresh leaves of fenugreek contain ascorbic acid of about 220.97 mg per 100 g of leaves and b-carotene is present about 19 mg/100 g. On the other side, it was reported that 84.94% and 83.79% ascorbic acid were reduced in sun and oven-dried fenugreek leaves respectively. Fresh leaves are used as vegetables in the diets. It was found that there was a better retention of nutrients in the leaves of fenugreek. The leaves of fenugreek should be stored in either in refrigeration conditions, or dried in oven, or blanched for sometime (about 5 min) and should be cooked in pressure cooker. 1.1.2. Seed Fenugreek is known for its pleasantly bitter, slightly sweet seeds. The seeds are available in any form whether whole or ground form is used to flavor many foods mostly curry powders, teas and spice blend. Fenugreek seed has a central hard and yellow embryo which is surrounded by a corneous A study was conducted on sweat of human after fenugreek ingestion and it has been concluded that compounds responsible for the strong maple-syrup odor present in sweat after fenugreek ingestion are due to the following components including the following: pinene; 3-octen-2-one, 2,5- dimethylpyrazine, b-; camphor; terpinen-4-ol; 4isopropylbenzaldehyde; neryl acetate and b-caryophyllene but it was observed that 2,5-dimethylpyrazine to be a major component responsible for sweat odor contributing compound (18). and comparatively large layer of white and semi-transparent endosperm (Betty, 2008). List of chemical constituents is shown in table below. The chemical composition of fenugreek (such as seeds, husk and cotyledons) showed that endosperm had the highest (4.63 g/100 g) saponin and (43.8 g/100 g) protein content. As against this, husk contains higher total polyphenols. The extracts of endosperm husk, and fenugreek seed at about 200 lg concentration exhibited antioxidant activity 72%, 64%, and 56% respectively by free-radical scavenging method [14].

The seeds of fenugreek contain about 0.1–0.9% of diosgenin and are extracted commercially. The structure of diosgenin is shown in Fig. 1. The plant tissue cultures from seeds of fenugreek when grown under optimal conditions have been found to produce as much as 2% diosgenin with smaller amounts of trigogenin and gitongenin. Seeds also contain the saponin (fenugrin B). Fenugreek seeds have been found to contain several coumarin compounds as well as a number of alkaloids (e.g., trigonelline, gentianine, carpaine). The large amount of trigonelline is degraded to nicotinic acid and related pyridines during roasting (15). The major bioactive compounds in fenugreek seeds are believed to be polyphenol compounds, such as rhaponticin and isovitexin (16) (Fig. 1). Small amount of volatile oils and fixed oil has been found in fenugreek seeds (17).

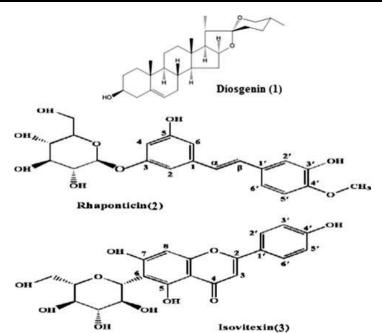


Fig. 1. The chemical structures of (1) Diosgenin (2) Rhaponticin and (3) Isovitexin.

Blank et al. (1997) have found the odor active compounds based compounds, sotolon was reported to be found most predominantly in (5s)-enantiomeric form (95%) in fenugreek. A list of chemical constituents is shown in Table 1 below

S. no.	Chemical constituents of fenugreek		
Alkaloids	Trimethylamine, Neurin, Trigonelline, Choline, Gentianine, Carpaine and Betain		
Amino acids	Isoleucine, 4-Hydroxyisoleucine, Histidine, Leucine, lysine, L- tryptophan, Arginine		
Saponins	Graecunins, fenugrin B, fenugreekine, trigofoenosides A–G		
Steroidal apinogens	Yamogenin, diosgenin, smilagenin, sarsasapogenin, tigogenin, neotigogenin, gitogenin, neogitogenin, yuccagenin, saponaretin		
Flavonoids	Quercetin, rutin, vitexin, isovitexin		
Fibers	Gum, neutral detergent fiber		
Lipids	Triacylglycerols, diacylglycerols, monoacylglycerols, phosphatidylcholine phosphatidylethanolamine, phosphatidylinositol, free fatty acids.		
Other	Coumarin, lipids, vitamins, minerals. 28% mucilage; 22% proteins; 5% of a stronger-swelling, bitter fixed oil.		

II. PHARMACEUTICAL BENEFITS OF FENUGREEK

Nature has been a source of medicinal treatments for thousands of years, and plant based systems continue to play an essential role in the primary health care of 80 % of the world's developing and developed countries [19]. According to the Ayurveda, plants have so many constituent which may be used for the treatment of so many diseases. Herbal drugs are easily available and have fewer side effects. People all over the world are now greatly attracted towards the herbal plant drugs. Fenugreek is easily available in our kitchen and use as drugs from oldest time. Fenugreek was used to ease childbirth and to increase milk flow, it is still traditionally used as remedy for various ailments, for instance it is taken by Egyptian women for menstrual pain and as hilba tea to ease stomach problems of tourists; Fresh fenugreek leaves for the treatment of indigestion, flatulence and a sluggish liver [20]. An infusion of the leaves is used as a gargle for recurrent mouth ulcers. A gargle made from the seeds is best for ordinary sore throat. Fresh Fenugreek leaves paste applied over the scalp regularly before bath helps hair grow, preserves natural color, keeps hair silky and also

cures dandruff; Fenugreek seeds made in gruel, given to nursing mothers increase the flow of milk; Topically, the gelatinous texture of fenugreek seed may have some benefit for soothing skin that is irritated by eczema or other conditions. It has also been applied as a warm poultice to relieve muscle aches and gout pain; Fenugreek seeds reduce the amounts of calcium oxalate in the kidneys which often contributes to kidney stones. Traditional Chinese herbalists used it for kidney problems and conditions affecting the male reproductive tract; Fenugreek is currently used as a source of the steroid diosgenin, one of its active constituents from which other steroids can be synthesized. These traditional uses have probably informed extensive study on this medicinal plant and the following biological activities have been associated with fenugreek in various studies: antidiabetic; antiplasmodic; hypolipidemic, antibacterial; anthelmintic; anti-inflammatory and analgesic activity; antioxidant, anticarcinogenic, antiulcer, antifertility, immunomodulatory effect, enzymatic pathway modifier, activities [21]. A list of pharmaceutical benefits of fenugreek is shown in Table 2.[22]

S.no.	Component used	Beneficial effects
1	Seeds	Hypoglycemic effect
2	Seeds	Hypocholesterolemic effect
3	Seed, leaves	Antioxidant
6	Seed	Lactation aid
9	Seed	Immunomodulatory effect
10	Seed	Digestive effect
11	Seeds and leaves	Decreases blood pressure
14	Seeds and leaves	Wounds and sore muscles treatment
15	Seeds, leaves	Anti-cancer agent
16	Seeds .	Asthma, emphysema, pneumonia
17	Seeds leaves	Anti-ulcer agent
19	Seed	Induces growth and reproduction hormones
20	Leaves and seeds	Gastro- and hepatoprotective
21	Seed	For healthy heart
23	Seed	Prevents constipation
24	Seed, leaves	Digestive and appetizer

Table 2. Nutraceutical properties of fenugreek

3.1 Antidiabetic activity

Preliminary animal and human trials suggest possible hypoglycaemic and antihyperlipidemic properties of fenugreek seed powder taken orally. Fenugreek has been well known to be used as antidiabetic remedy for both type I and II diabetes andhas been extensively used as a source of antidiabetic compounds, from its seeds, leaves and extracts in different model systems [23, 24] About 25-50 g fenugreek seeds were given to diabetic patients daily in diet to prevent and manage long term complications of diabetes and studies have been made about the glycemic index of fenugreek recipes which showed that the soluble fenugreek fiber has significantly reduced the glycemic potential and for this reason it may be used as a supplementary medicine to treat the diabetic population by significantly reducing the dose of standard drugs. Since fenugreek seeds are a source of protein, they can replace pulses in the diets of diabetics. 25-50 g fenugreek in the diet of diabetic patients (taken daily) can be an effective supportive therapy in the

management of diabetes [26]. The bioactive compounds with respect to diabetic conditions include the galactomannan-rich soluble fiber fraction of fenugreek which may be responsible for the antidiabetic activity of the seeds [27].

3.2 Antilipidemic activity

Fenugreek seeds have been shown to exhibit hypocholesterolemic effects, lowered serum cholesterol, triglyceride and low-density lipoprotein in hypercholesterolemia suffering patients and experimental models [28]. In obesity suffering rats fenugreek consumption in diet reduced triglyceride accumulation in the liver while fecal bile acid and cholesterol excretion were increased by fenugreek administration. This may be secondary to a reaction between the bile acids and fenugreek derived saponins causing the formation of micelles too large for the digestive tract to absorb.

3.3 Antioxidant activity

Fenugreek contains phenolic and flavonoid compounds which help to enhance its antioxidant capacity [29]. It has been suggested that fenugreek has powerful antioxidant property that has beneficial effect on liver and pancreas; since antioxidant properties have been linked to health benefits of natural products; such properties are studied with germinated fenugreek seeds which are observed to be more beneficial than dried seeds because of the fact that germinated seed increases the bioavailability of different constituents of fenugreek [30]. An aqueous fraction of

fenugreek exhibits the highest antioxidant activity compared to other fractions and the quantity of phenolic and flavonoid compounds are related to antioxidant activity. Studies have revealed significant antioxidant activity in germinated fenugreek seeds which may be due to the presence of flavonoids and polyphenols. Furthermore, mustard and fenugreek seeds showed hypoglycemic and antihyperglycemic activity in diabetic mice and this may be due to the presence of antioxidant carotenoids in those spices [31].

3.4 Anticancer perspectives

One of the primary causes of death nowadays is cancer in the world. Serious side effects occur with generally used therapeutic medicines which only increase the life span of patient from few months or some years. Plantbased active components have shown their potential to be used as suitable and safe alternatives having significantly explored anticancer effects.[32] In this regard, active ingredients of vegetables and fruits are being utilized to prevent the chances of cancer.[33] Efforts are ongoing to use the other approaches and ideas which can be effective in the prevention of cancer. In these attempts, studies are available in which animals and cell lines were used as the investigational models of cancer proved the effect of seeds of fenugreek against cancer.[34]

It was revealed that a compound protodioscin derived from fenugreek exhibits an effect to inhibit the growth against HL60 cells by prompting apoptotic modifications.[35] In another study, extract from the seeds of fenugreek expressively stop the mammary hyperplasia induced by 7,12- dimethylbenz-anthracene and diminished the occurrence of it in rats. It is recommended that increased apoptosis after this edible herb consumption shows effect against breast cancer. The extract of the whole plant of fenugreek (Trigonella foenum-graecum) exhibit the cytotoxicity effect in vitro against the most of the different types of cancer cell lines in human like a neuroblastoma, IMR-32 and HT29 cancer cell line.[36]

Researchers inspected the outcome of extracts of fenugreek (aqueous as well as ethanol) on the development of breast cancer cell line (an estrogen receptor), MCF-7 cells and stated as decreased mitochondrial membrane potential and inversion of phosphatidylserine by the early apoptotic changes and decreased cell viability after the consumption of ethanol extract. Further, when DNA splits into more pieces comprising many of approximately 180–200 base pair has also been witnessed.[37]

In another study, the anti-cancer properties of fenugreek extract were investigated against breast, pancreatic and prostate cancers. The findings exposed that the applied extract was effective in inhibiting the growth of cancer cell lines of pancreatic and breast cancers however, no effect was shown on primary or immortalized prostate cells. The possible mechanism for anti-cancer properties of Trigonella foenum graecum extract was the induction of programmed cell death.[38]

In Balb-C mice model of Ehrlich ascites carcinoma (EAC), extract of the seed of fenugreek shows the effect against the neoplastic. In mice when the alcohol extract of the fenugreek was administered before and after injection of EAC cell, there was the 70% reduction in tumour cell growth.[26] The extract of fenugreek exhibits a noteworthy effect against the inflammation and improved macrophage cells count as well as peritoneal ooze cells count.[39]

Fenugreek seed's ability to lessen hepatic oxidative stress and its antioxidant properties were applied in wistar rats with colon cancer which is induced by 1,2-dimethylhydrazine (DMH). 100% colon tumor was induced by treating them with DMH also showed the increased lipid peroxidation and in the liver-reduced glutathione amount, catalytic activity, glutathione peroxidase, glutathione transferase and sphincte-r of oddi dysfunction. The food consist of the seed powder of fenugreek abridged tumor in colon occurrence and lipid peroxidation in DMH-treated rats and in liver it also amplified activities of catalase, glutathione peroxidase, sphincter of oddi dysfunction and glutathione transferase.[40]

3.5 Effect of Trigonella against pulmonary fibrosis

Pulmonary fibrosis is one of the primary lungs disease in which stiffening and damaging of lungs tissues take place Asththat ultimately results in improper breathing. The study was designed to clarify the oxidation reduction balance and mechanism of inflammation relationship in pulmonic fibrosis. The pulmonic structure is predominantly susceptible to reactive oxygen species prompted damage due to its constant contact to poisonous contaminants. Rats were treated with BLM firstly to make a tentative experimental unit of pulmonic fibrosis, then the aqueous acetonic extract and powder supplementation of the seeds of fenugreek to check its potential as anti-inflammatory and antioxidant. The main outcome that was observed is fenugreek has useful properties by constraining inflammatory reaction and peroxidation of lipid in fibrosis pulmonic. Nonetheless additional studies on the seeds of fenugreek are needed to be prepared to clarify its molecular mechanism. Therefore, the different treatments that contain antioxidants could add to forthcoming real remedies of pulmonic fibrosis.[41] It is the need of time to add the fenugreek in our daily diet, for its high nutritional profile as well as it can help in avoidance of pulmonic fibrosis, even if it is of unidentified aetiology.

3.6 Fenugreek against obesity

Several investigations report that hydroxyl isoleucine ameliorates insulin resistance caused by obesity. Researchers proposed that hydroxyl isoleucine down-regulated a tumour necrotic factor-transforming catalyst which causes the change of mTNF to sTNF. The studies also provide the information about the pathway of signal transduction and upgraded the insulin confrontation, which is induced by obesity in adipocytes (3T3-L1).[42] Alike findings have been described in Zucker rats, which were obese given the seeds of fenugreek. Researcher experiments the livers of the rats which were obese, the decrease in tumour necrosis factor intensities, important rise in receptors of membrane and TNF receptor 2. In additional research, it was demonstrated that fibre present in fenugreek ominously suppresses the hunger and amplifiedin obese experimental units. Dietary supplementation of fenugreek is proved to have significant effect on loss of weight for short period of time.[43] When the fenugreek powder was given to obese rats for 14 weeks, they noticed the change in nutritional values, body measurements and decrease in the body weight was detected. Galactomannan that is present in the seeds of fenugreek capture and excrete the sugars from body before it moves in the blood, this causes the loss of weight.[44]

When aqueous fenugreek extracts were given to high-fat-fed rats, they reported noteworthy decrease in the weight of body, as well as in body mass index and drop in serum lipid profile and cardiac hazard elements. Leptin levels in the adipose tissue are reduced by the fenugreek to control the appetite.[45] Similar interpretations were prepared in rats that were obese due to monosodium glutamate.[46] In mice, the activity of furanostolic saponins (FenfuroTM) obtained from fenugreek on the insulin resistance was assessed. The results concluded that administration of FenfuroTM reduced the phosphorylation of protein kinase B stimulated by insulin. FenfuroTM also dropped the assembly of fat and better insulin sensitivity and glucose acceptance.[47] It can be proved very useful in weight loss without any major side effect.

3.7 Fenugreek in asthma treatment

Asthma is one of the most prevailing lungs disorder in which the bronchial tubes or airways become inflammed and tightened the pathway for inhalation and exhalation of air. To treat the mild asthma, the study was conducted to check the safety and efficiency of the extract of the seeds of when used as supplement. TPM formula was used by adding the syrup of fenugreek in honey solution. In comparison with the placebo and honey syrup, the aqueous extract of the seeds of fenugreek amended the Quality of Life and the tests of lung functioning in patients having mild asthma. Extract of the seed of fenugreek when used, it headed to a ten percent (10%) rise in FEV1 (forced expiratory volume in one second) and FEV1/FVC heights, in calculation of an imperative decline in serum cytokine IL-4 heights. By the findings of study, it can be suggested that in the treatment of mild asthma, use of the aqueous extract of fenugreek can prove beneficial just with the few side effects. Fenugreek was nominated amongst TPM treatments. During the study, once picking simple

grouping to perceive fenugreek special effects or side effects more closely, agreeing to TPM, fenugreek works to better functioning of lung as helps the lung secretions and as a lung tonic.[48]

In the fenugreek, the polyphenols having low molecular weight known as flavonoids are the major part, which are active during the treatment of asthma and play the role against asthma to some extent. In different studies, due to the presence of flavonoids in fenugreek, it shows the antioxidant effects by constraining the lipid peroxidation and guard the airways from the stress of oxidation.[49] Stimulation of mast cells and basophils are also interrupted by the flavonoids.[50] Fenugreek has antioxidant influence along with the presence of a flavonoid named as quercetin, which can stop the formation of crystals of Charcot-Leyden, and eosinophil cationic proteins that cause the pathogenesis in asthma. Fenugreek likewise has the capacity to decrease the injury triggered by oxidative mediators.[51] Different stages such as the formation of micro capillary tubule and cell migration in the angiogenesis can be prevented by the flavonoids.[52] As exposed in prior researches, in asthma pathogenesis the changes in vascular plays a significant role .[53] It has been confirmed that the seeds of fenugreek have the distinct effect as an anti-inflammatory.[54] Recovered asthmatic cough and comfort in the secretions of lungs are achieved because of the presence of 28% mucilage component of fenugreek seeds, this is the additional conceivable mechanism of act of fenugreek.[54] In atrophy and asthma problem, the both IL4 was chosen as Th2 profile to check the position of the association between the imbalance of cytokine (Th1/Th2).[55] The efficacy of the fenugreek was much better than honey. when both fenugreek and honey was used in the process of treatment to reduce the IL4 levels. Swelling of airway and synthesis of Ig-E could be happened when IL4 separated after T lymphocytes and mast cells.[56] Other studies resolute the consequence of interleukin4 antibodies, interleukin5 antibodies, interleukin13 antibodies in asthma pathogenesis therefore production balances among TH1 and TH2 cytokines could be supportive in management of asthma.[57] Trigonella foenum graecum has an extensive range of dosage. 25 g of powdered seed of fenugreek was finely endured and no side effect was seen, in a human study.[56] Acute injuriousness values (LD50) recognized for fenugreek are 5 gram/kg in rats when given orally and 2 gram/kg in rabbit use as dermal from extract of alcoholic seed. The following important subject of the study was the part of honey. Decrease level of IL4, improved lung function, increase the Quality of Life, in the outcomes showed when honey syrup was used for the patients of asthma. When the fenugreek and honey syrups are used in combination, it accelerated the efficacy of formula but when used separately, the result of fenugreek syrup was better than that of honey syrup. Honey is used in many treatments of TPM as a protective agent, but in lung diseases, it also plays more beneficial role.[48]

At the end, in the primary study when the honey-based syrup of aqueous extract of Trigonella foenum graceum (Fenugreek) was used as supplement in the treatment of mild asthma, it exhibited the satisfactory results. In the treatment of mild asthma, fenugreek syrup therapy can be recommended as adjuvant therapy, due to upright consequences and sound forbearance of the syrup of fenugreek.[55] From the different studies, it can be concluded that the daily use of fenugreek can help to avoid the symptoms of asthma. It also helps in improving the function of lungs and respiratory tract as it acts as tonic. In spite of the efficiency of the seeds of fenugreek established through the study, the main mechanism involved behind its effectiveness is still mysterious, and more researches and studies based on the multiple samples are required.

3.8 Immunomodulatory effect

An agent that intensifies or diminishes the immune responses is known as immunomodulator and such effect is called

As immunomodulatory effect. Immunomodulatory substance interferes with three basic areas of the immune responses directly or indirectly; the mucosal barrier function, the cellular defense function and the local or systemic Inflammatory response. Research work in this effect of fenugreek is scanty but stimulatory immunomodulatory effect has been shown (as evidenced from body weight, relative thymus weight, cellularity of lymphoid organs, delayed type of hypersensitivity response, plaque forming cell assay, haemagglutination titre, quantitative haemolysis assay, phagocytosis, lymph proliferation and a significant increase in phagocytic index and phagocytic capacity of macrophages) of aqueous extract of fenugreek at three doses 50, 100 and 200mg per kg of body weight for 10 days on the immune system of Swiss albino mice [58].

3.9 Regulation of Fat Metabolism

Obesity is a long-term carbohydrate and lipid metabolic condition marked by excessive fat accumulation in adipose tissue and other internal organs. Insulin resistance, type 2 diabetes, coronary heart disease, cancer, and respiratory disorders are all linked to obesity [59]. Many drugs have been used to treat obesity over the years, but the majority of them have now been removed due to harmful side effects. Fenugreek

has been demonstrated in several trials to have anti-obesity characteristics, making it a promising plant option for treating obesity. Fenugreek has a great deal of soluble fibre, which helps to speed up weight reduction by improving digestion and metabolism. Galactomannan, a water-soluble fibre contained in fenugreek seeds, suppresses hunger by increasing the sense of fullness, which aids weight loss. Overall, it enhances glucose and lipid metabolism, insulin sensitivity, antioxidant defence, and lipogenic enzyme downregulation [60]. In vivo, diosgenin may also decrease cholesterol production. The mechanisms of saponins in dyslipidemiaameliorating actions were initially explained by accelerating cholesterol metabolism and reversing cholesterol transport, as well as blocking 3-hydroxy-3-methylglutaryl coenzyme A reductase in serum and liver [61].

3.10 Neuroprotective Effect

Neurological illnesses, such as neuropathic pain, are among the most common, and empirical data show that inflammatory cytokines and microglial cells play a role in the aetiology of neuropathic pain [62]. Using animal models, researchers have revealed the potential benefits of medicinal herbs for the treatment of neurological illnesses. Fenugreek has also been investigated as a potential medicinal herb for the treatment of neurological illnesses in this respect. Khalil et al. [63] fed rats fenugreek saponins (0.05–2.0%) for 45 days and discovered that the dietary treatment of fenugreek-saponins-inhibited apoptosis and acetylcholinesterase (AChE) activity resulted in neuroprotective benefits. Similarly, Bin-Hafeez et al. [64] used a mouse model to study the neuroprotective effects of 5% fenugreek seed powder on aluminium-chloride-induced neurotoxicity and found that fenugreek seed powder had a substantial neuroprotective impact. Trigonella (100 mg/kg) has also been shown to play a function in lowering the risk of Parkinson's disease by avoiding rotational behaviour and restoring SNC (substantia nigra compact) neuron and MDA (malondialdehyde) levels [65].

3.11 Heart and Gastro Protective

Fenugreek helps to prevent irregular blood clotting by reducing platelet aggregation. This entire process is linked to heart attacks and strokes. In animal research, it was discovered that fenugreek reduced myocardium damage and oxidative stress during isoproterenol-induced myocardial infarction Due to the presence of flavonoids and sulfhydryl, fenugreek is used to cure ulcers [66]. Sulfhydryl protects mucosa from ulcerative lesions caused by a variety of necrotic causes. The presence of sulfhydryl causes an increase in gastric mucosa, which aids the anti-ulcer properties of fenugreek seeds. The Sulfhydryl molecule is an antioxidant that helps to maintain the stomach's mucosal integrity [67,68].

3.12 Improve Sexual and Galactogogue

Functions Several experiments have been conducted in order to address these issues. Jiayou Materia's trial revealed that fenugreek helps with kidney problems and a variety of other disorders. In mice, the liquid extract of fenugreek increases sperm mortality and cation sperms channel proteins. Sixty fit individuals between the ages of 25 and 52 participated in a six-year study. They came to the conclusion that fenugreek seeds improved male sexual functioning, improved sexual life, and regulated orchid hormones and lactogen. After 6 years of research, it was shown that giving 1200 women 2-3 fenugreek tablets (580-610mg) three times a day causes them to produce more breast milk in 1 to 3 days [69].

III. CONCLUSION

In the present review, attempt has been made to elaborate on the reported pharmacological uses of fenugreek. Herbs are utilised medicinally in a variety of countries owing to the widespread idea that natural items have no side effects and are readily available. In this overview, the physical and chemical properties of fenugreek, as well as traditional usage and pharmacological effects discovered in diverse investigations, are described. Additionally, the clinical applications of fenugreek are also attributed to its diverse chemical composition, which make this plant a strong to alleviate the dependence on various synthetic drugs for curing the diseases. However, further research is needed to explore the modern isolation techniques for bioactive components for the development of novel functional foods and drugs. Moreover, economically feasible molecular farming approaches based on microbial bioreactors should also be studied to synthesize the recombinant pharmaceutical proteins by using the in vitro cultured plant cells. Likewise, proper investigations consisting of well-planned clinical studies are direly needed to produce prosperous results for the mankind.

IV. ACKNOWLEDGMENT

The authors are grateful to the principal (Prof. M. Ganga Raju) and management of the Gokaraju Rangaraju College of pharmacy, for the constant support and encouragement during the course of work.

REFERENCES

- [1] Fenugreek seeds. Available from: http://chestofbooks.com/health/materia-medicadrugs/Textbook-Materia-Medica/Fenugreek-Seeds-Semina-Foeni-Graeci.html
- [2] Flammang AM, Cifone MA, Erexson GL, Stankowski LF. Genotoxicity testing of Fenugreek extract. Food and Chemical Toxicology. 2004; 42: 1769–1775.
- [3] Ayurvedic herb fenugreek. Available from: http://www.indianmirror.com/ayurveda/fenugreek.html
- [4] Botinical.com. fenugreek. available from: http://www.botanical.com/botanical/mgmh/f/fenugr07.html#des
- [5] Herbs at a glance. U.S. Department of Health and Human Services. Available from: www.ods.od.nih.gov
- [6] Syeda BB, Muhammad I B, Shahabuddin M. Antioxidant activity from the extract of fenugreek seeds. Pak. J. Anal. Environ. Chem. 2008; 9(2): 78 83.
- [7] Srivastava, A.; Singh, Z.; Verma, V.; Choedon, T. 2020. Potential Health Benefits of Fenugreek with Multiple Pharmacological Properties. In Ethnopharmacological Investigation of Indian Spices, Mishra, N., Ed., 137–153. IGI Global, Hershey, Pennsylvania, USA. doi:http://doi:10.4018/978-1-7998-2524-1.ch011.
- [8] Aasim, M.; Baloch, F. S.; Nadeem, M. A.; Bakhsh, A.; Sameeullah, M.; Day, S. Fenugreek (*Trigonella foenum-graecum* L.): An Underutilized Edible Plant of Modern World. In Global Perspectives on Underutilized Crops; Ozturk, M., Hakeem, K., Ashraf, M., Ahmad, M., Eds.; Springer: Cham, 2018, 381–408.
- [9] Reddy, R. L. R.; Gowda, A. N. S.; Srinivasan, K. Antilithogenic and Hypocholesterolemic Effect of Dietary Fenugreek Seeds (Trigonella Foenum-graecum) in Experimental Mice. Medicinal Plants. Int. J. Phytomed. Related Ind. 2019, 11, 145–154.
- [10] Wani, S. A.; Kumar, P. Fenugreek: A Review on Its Nutraceutical Properties and Utilization in Various Food Products. J. Saudi Society Agri. Sci. 2018, 17, 97–106.
- [11] Khare CP, editor. Indian herbal remedies: rational Western therapy, ayurvedic, and other traditional usage, Botany. Springer science & business media; 2004.
- [12] Rao AV. Herbal cure for common diseases. Diamond Pocket Books (P) Ltd.; 2004.
- [13] Yadav SK, Sehgal S. Effect of home processing and storage on ascorbic acid and β-carotene content of bathua (Chenopodium album) and fenugreek (Trigonella foenum graecum) leaves. Plant foods for human nutrition. 1997 May;50:239-47.
- [14] Naidu MM, Shyamala BN, Naik JP, Sulochanamma G, Srinivas P. Chemical composition and antioxidant activity of the husk and endosperm of fenugreek seeds. LWT-Food Science and technology. 2011 Mar 1;44(2):451-6.
- [15] Acharya S, Srichamroen A, Basu S, Ooraikul B, Basu T. Improvement in the nutraceutical properties of fenugreek (*Trigonella foenum-graecum* L.). Songklanakarin J. Sci. Technol. 2006;28(1):1-9.
- [16] He Y, Ding C, Wang X, Wang H, Suo Y. Using response surface methodology to optimize countercurrent chromatographic separation of polyphenol compounds from fenugreek (*Trigonella foenum-graecum* L.) seeds. Journal of Liquid Chromatography & Related Technologies. 2015 Jan 2;38(1):29-35.
- [17] Sowmya P, Rajyalakshmi P. Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. Plant Foods for Human Nutrition. 1999 Dec;53:359-65.
- [18] Meghwal M, Goswami TK. A review on the functional properties, nutritional content, medicinal utilization and potential application of fenugreek. Food Processing & Technology. 2012.
- [19] King H Aubert RE and Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998; 21: 1414-1431.
- [20] Basch E Ulbricht C Kuo G Szapary P and Smith M. Therapeutic applications of fenugreek. Altern. Med. Rev. 2003; 8: 20-27.
- [21] Hannana JMA Rokeya B Faruque O Nahar N Mosihuzzaman M Khana AK and Alia L. Effect of soluble dietary fiber fraction of *Trigonella foenum-graecum* on glycemic, insulinemic, lipidemic and platelet aggregation status of Type 2 diabetic model rats. J. Ethnopharmacol. 2003; 88: 73-77.
- [22] Wani SA, Kumar P. Fenugreek: A review on its nutraceutical properties and utilization in various food products. Journal of the Saudi Society of Agricultural Sciences. 2018 Apr 1;17(2):97-106.
- [23] Raju J Gupta D Rao AR Yadava PK and Baquer NZ. Trigonella foenum graecum (fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. Mol. Cell Biochem. 2001;224: 45-51.

- [24] Khalki L M'hamed SB Bennis M Chait A and Sokar Z. Evaluation of the developmental toxicity of the aqueous extract from *Trigonella foenum-graecum* (L.) in mice. J. Ethnopharmacol. 2010; 15: 321-325.
- [25] Sowmya P, Rajyalakshmi P. Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. Plant Foods for Human Nutrition. 1999 Dec;53:359-65.
- [26] Senthil A, Mamatha BS, Vishwanath P, Bhat KK, Ravishankar GA. Studies on development and storage stability of instant spice adjunct mix from seaweed (Eucheuma). Journal of food science and technology. 2011 Dec;48:712-7.
- [27] Rashmi Yadav RY, Rahul Kaushik RK. A study of phytochemical constituents and pharmacological actions of Trigonella foenum-graecum: A review. 2011
- [28] Mathern JR, Raatz SK, Thomas W, Slavin JL. Effect of fenugreek fiber on satiety, blood glucose and insulin response and energy intake in obese subjects. Phytotherapy research. 2009 Nov;23(11):1543-8.
- [29] Dixit P, Ghaskadbi S, Mohan H, Devasagayam TP. Antioxidant properties of germinated fenugreek seeds. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2005 Nov;19(11):977-83.
- [30] Altuntaş E, Özgöz E, Taşer ÖF. Some physical properties of fenugreek (Trigonella foenum-graceum L.) seeds. Journal of food engineering. 2005 Nov 1;71(1):37-43.
- [31] Jk G. Medicinal plants of India with antidiabetic potential. J Ethnopharmacol.. 2002;81:81-100.
- [32] Mohammadinejad, R.; Shavandi, A.; Raie, D. S.; Sangeetha, J.; Soleimani, M.; Hajibehzad, S. S.; Thangadurai, D.; Hospet, R.; Popoola, J. O.; Arzani, A.; et al. Plant Molecular Farming: Production of Metallic Nanoparticles and Therapeutic Proteins Using Green Factories. Green Chem. 2019.
- [33] Tohidi, B.; Rahimmalek, M.; Arzani, A. Essential Oil Composition, Total Phenolic, Flavonoid Contents, and Antioxidant Activity of Thymus Species Collected from Different Regions of Iran. Food Chem. 2017, 220, 153–161.
- [34] Yadav, U. C.; Baquer, N. Z. Pharmacological Effects of *Trigonella foenum-graecum* L. In Health and Disease. Pharm. Biol. 2014, 52, 243–254.
- [35] Hibasami, H.; Moteki, H.; Ishikawa, K.; Katsuzaki, H.; Imai, K.; Yoshioka, K.; Ishii, Y.; Komiya, T. Protodioscin Isolated from Fenugreek (Trigonella Foenumgraecum L.) Induces Cell Death and Morphological Change Indicative of Apoptosis in Leukemic Cell Line H-60, but Not in Gastric Cancer Cell Line KATO III. Int. J. Mol. Med. 2003, 11, 23–26.
- [36] Verma, S. K.; Singh, S. K.; Mathur, A. In Vitro Cytotoxicity of Calotropis Procera and Trigonella foenum-graecum against Human Cancer Cell Lines. J. Chem. Pharm. Res. 2010, 2, 165–861.
- [37] Sebastian, K. S.; Thampan, R. V. Differential Effects of Soybean and Fenugreek Extracts on the Growth of MCF-7 Cells. Chem. Biol. Interact. 2007, 170, 135–143.
- [38] Shabbeer, S.; Sobolewski, M.; Anchoori, R. K.; Kachhap, S.; Hidalgo, M.; Jimeno, A.; Davidson, N. E.; Carducci, M.; Khan, S. R. Fenugreek: A Naturally Occurring Edible Spice as an Anticancer Agent. Cancer Boil. Ther. 2009, 8, 272–278.
- [39] Sur, P.; Das, M.; Gomes, A.; Vedasiromoni, J. R.; Sahu, N. P.; Banerjee, S.; Sharma, R. M.; Ganguly, D. K. Trigonella Foenum Graecum (Fenugreek) Seed Extract as an Antineoplastic Agent. Phytother. Res. 2001, 15, 257–259.
- [40] Devasena, T.; Menon, P. V. Fenugreek Seeds Modulate 1, 2-dimethylhydrazine-induced Hepatic Oxidative Stress during Colon Carcinogenesis. Ital. J. Biochem. 2007, 56, 28–29.
- [41] Yacoubi, L.; Rabaoui, L.; Hamdaoui, M. H.; Fattouch, S.; Serairi, R. B.; Kourda, N.; Khamsa, S. B. Anti-oxidative and Anti-inflammatory Effects of *Trigonella foenum-graecum* Linnaeus, 1753 (Fenugreek) Seed Extract in Experimental Pulmonary Fibrosis. J. Med. Plants Res. 2011, 5, 2325– 4315.
- [42] Gao, F.; Du, W.; Zafar, M. I.; Shafqat, R. A.; Jian, L.; Cai, Q.; Lu, F. 4-Hydroxyisoleucine Ameliorates an Insulin Resistant-like State in 3T3-L1 Adipocytes by Regulating TACE/TIMP3 Expression. Drug Des. Devel. Ther. 2015, 9, 5727–5728.
- [43] Raju, J.; Bird, R. P. Alleviation of Hepatic Steatosis Accompanied by Modulation of Plasma and Liver TNF-α Levels by Trigonella Foenum Graecum (Fenugreek) Seeds in Zucker Obese (Fa/fa) Rats. Int. J. Obes. 2006, 30, 1298–1307.
- [44] Mathern, J. R.; Raatz, S. K.; Thomas, W.; Slavin, J. L. Effect of Fenugreek Fiber on Satiety, Blood Glucose and Insulin Response and Energy Intake in Obese Subjects. Phytother. Res. 2009, 23, 1543– 1548.

- [45] Kumar, P.; Bhandari, U.; Jamadagni, S. Fenugreek Seed Extract Inhibit Fat Accumulation and Ameliorates Dyslipidemia in High Fat Diet-induced Obese Rats. BioMed Res. Int. 2014, 2014, 1– 11.[52] Kumar, P.; Bhandari, U. Fenugreek Seed Extract Prevents Fat Deposition in Monosodium Glutamate (Msg)-obese Rats. Drug Res. 2016, 66, 174–180.
- [46] Kumar, P.; Bhandari, U. Fenugreek Seed Extract Prevents Fat Deposition in Monosodium Glutamate (Msg)-obese Rats. Drug Res. 2016, 66, 174–180.
- [47] Hua, Y.; Ren, S. Y.; Guo, R.; Rogers, O.; Nair, R. P.; Bagchi, D.; Swaroop, A.; Nair, S. Furostanolic Saponins from *Trigonella foenum-graecum* Alleviate Diet-induced Glucose Intolerance and Hepatic Fat Accumulation. Mol. Nutr. Food Res. 2015, 59, 2094–2100.
- [48] Razi, M.;. Al-Havi (The Large Comprehensive); Dare Ehia Attorath Al Arabi: Beirut, 2001.[55] Schroeter, H.; Boyd, C.; Spencer, J. P.; Williams, R. J.; Cadenas, E.; Rice-Evans, C. MAPK Signaling in Neurodegeneration: Influences of Flavonoids and of Nitric Oxide. Neurobiol. Aging. 2002, 23, 861– 880.
- [49] Schroeter, H.; Boyd, C.; Spencer, J. P.; Williams, R. J.; Cadenas, E.; Rice-Evans, C. MAPK Signaling in Neurodegeneration: Influences of Flavonoids and of Nitric Oxide. Neurobiol. Aging. 2002, 23, 861– 880.
- [50] Naidu, M. M.; Shyamala, B. N.; Naik, J. P.; Sulochanamma, G.; Srinivas, P. Chemical Composition and Antioxidant Activity of the Husk and Endosperm of Fenugreek Seeds. LWT-Food Sci. Tech. 2011, 44, 451–456.
- [51] Mahabady, M. K.; Gholami, M. R.; Varzi, H. N.; Zendedel, A.; Doostizadeh, M. 2016. Protective Effect of Quercetin on Skeletal and Neural Tube Teratogenicity Induced by Cyclophosphamide in Rat Fetuses. Veterinary Research Forum, 7(2), 133-138
- [52] Boots, A. W.; Haenen, G. R.; Bast, A. Health Effects of Quercetin: From Antioxidant to Nutraceutical. Eur. J. Pharm. 2008, 585, 325–337.
- [53] Park, H. S.; Kim, S. Y.; Kim, S. R.; Lee, Y. C. Targeting Abnormal Airway Vascularity as a Therapeutical Strategy in Asthma. Respirology. 2010, 15, 459–471.
- [54] Sharififar, F.; Khazaeli, P.; Alli, N. In Vivo Evaluation of Anti-inflammatory Activity of Topical Preparations from Fenugreek (*Trigonella foenum-graecum* L.) Seeds in a Cream Base. Iran. J. Pharm. Sci. 2009, 5, 157–162.
- [55] Emtiazy, M.; Oveidzadeh, L.; Habibi, M.; Molaeipour, L.; Talei, D.; Parvin, M.; Kamalinejad, M. Investigating the Effectiveness of the *Trigonella foenum-graecum* L. (Fenugreek) Seeds in Mild Asthma: A Randomized Controlled Trial. Allergy Asthma Clin. Immunol. 2018, 14, 19–20.
- [56] [62] Vijayakumar, M. V.; Bhat, M. K. Hypoglycemic Effect of a Novel Dialysed Fenugreek Seeds Extract Is Sustainable and Is Mediated, in Part, by the Activation of Hepatic Enzymes. Phytother. Res. 2008, 22, 500–505
- [57] Busse, W. W.; Rosenwasser, L. J. Mechanisms of Asthma. J. Allergy Clin. Immunol. 2003, 111, 799– 804.
- [58] Raju J, Bird RP. Alleviation of hepatic steatosis accompanied by modulation of plasma and liver TNFα levels by Trigonella foenum graecum (fenugreek) seeds in Zucker obese (fa/fa) rats. International Journal of Obesity. 2006 Aug;30(8):1298-307.
- [59] McCarthy M. Genomics, Type 2 Diabetes, and Obesity. N. Engl. J. Med. 2010;363:2339–2350. doi: 10.1056/NEJMra0906948. [PubMed] [CrossRef] [Google Scholar]
- [60] 52. Kumar P., Bhandari U., Jamadagni S. Fenugreek Seed Extract Inhibit Fat Accumulation and Ameliorates Dyslipidemia in High Fat Diet-Induced Obese Rats. BioMed Res. Int. 2014;2014:606021. doi: 10.1155/2014/606021. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [61] 53. Achari A.E., Jain S.K. Adiponectin, a Therapeutic Target for Obesity, Diabetes, and Endothelial Dysfunction. Int. J. Mol. Sci. 2017;18:1321. doi: 10.3390/ijms18061321. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [62] 54. Soleimani M., Sheikholeslami M.A., Ghafghazi S., Pouriran R., Parvardeh S. Analgesic effect of α-terpineol on neuropathic pain induced by chronic constriction injury in rat sciatic nerve: Involvement of spinal microglial cells and inflammatory cytokines. Iran. J. Basic Med. Sci. 2019;22:1445–1451. doi: 10.22038/IJBMS.2019.14028. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [63] 55. Khalil W., Roshdy H., Kassem S. The potential therapeutic role of Fenugreek saponin against Alzheimers disease: Evaluation of apoptotic and acetylcholinesterase inhibitory activities. J. Appl. Pharm. Sci. 2016;6:166–173. doi: 10.7324/JAPS.2016.60925. [CrossRef] [Google Scholar]

- [64] Bin-Hafeez B., Haque R., Parvez S., Pandey S., Sayeed I., Raisuddin S. Immunomodulatory effects of fenugreek (Trigonella foenum graecum L.) extract in mice. Int. Immunopharmacol. 2003;3:257– 265.
- [65] 56. Foltynie T., Kahan J. Parkinson's disease: An update on pathogenesis and treatment. J. Neurol. 2013;260:1433–1440. doi: 10.1007/s00415-013-6915-1.
- [66] Murugesan MRR. Cardioprotective effect of fenugreek on isoproterenol-induced myocardial infarction in rats. Indian J Pharmacol. 2011;516–519. 58.
- [67] López A, The role of gastric mucosal sulphydryls in the ulcer-protecting sulphydryls in the ulcer-protecting. The Journal of The Journal of pharmacy and pharmacology. 1996;37-40.
- [68] Choi SM, SJ. Gastroprotective effects of DA-6034, a new flavonoid derivative, in various gastric mucosal damage models. Dig Dis Sci. 2007;3075-3080.
- [69] Huggins. Fenugreek: One remedy for low milk production. Rental Roundup. 1998;16-7.

